WOUND HEALLING

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WOUND HEALLING

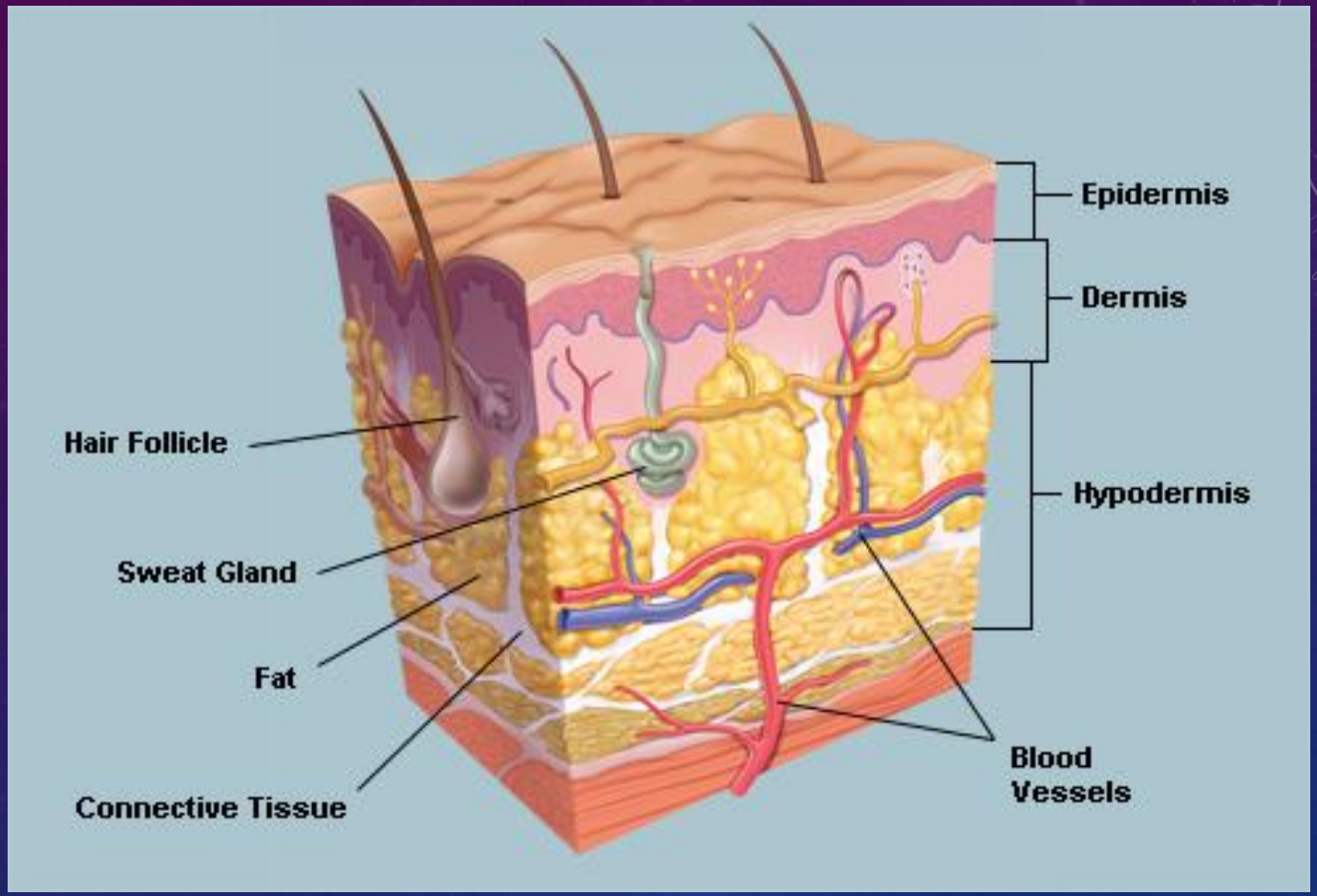
- Wounds
- Wound healling
- Classification of wounds
- Type of wound closure
- Phases of healing
- Growth factors in wound healing
- scars

WOUND HEALING

- Wound:
  - Disruption of the normal continuity of body structure
- Healling:
  - Summation of a number of processes by which new tissue [scar] is formed following injury to restore tissue integrity

ANATOMY OF THE SKIN

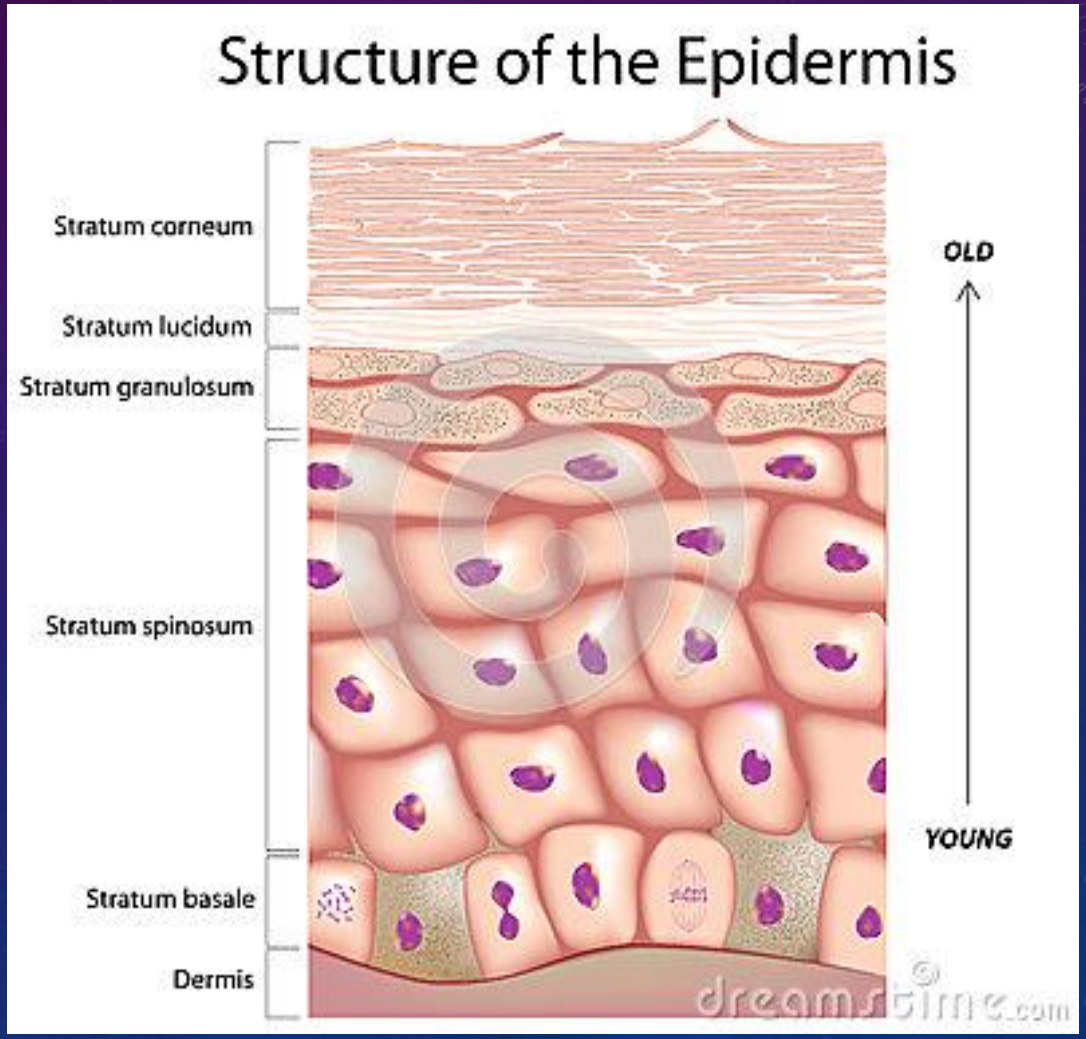
- The skin is the largest organ of the body
- Skin has three layers:
  - The epidermis
  - The dermis
  - The deeper subcutaneous tissue (hypodermis)


Epidermis
Dermis
Hypodermis
Hair Follicle
Sweat Gland
Fat
Connective Tissue
Blood Vessels

ANATOMY OF THE SKIN

- The epidermis
  - The principal cell of the epidermis is called a keratinocyte.
  - a keratinocyte gradually migates to the surface and is sloughed off in a process called desquamation.
  - The epidermis is subdivided into five layers or strata
    - the stratum basale
    - the stratum spinosum
    - the stratum granulosum
    - the stratum lucidum
    - the stratum corneum

ANATOMY OF THE SKIN



ANATOMY OF THE SKIN

- The dermis
  - thermoregulation and supports the vasular network to supply the avascular epidermis with nutrients.
  - subdivided into two zones,
    - papillary dermis
    - reticular layer
  - The dermis contains mostly fibroblasts which are responsible for secreting collagen, elastin and ground substance that give the support and elasticity of the skin.
  - Also present are immune cells that are involved in defense against foreign invaders passing through the epidermis.

CLASSIFICATION OF WOUNDS:

- Acute:
  - Penetrating: surgical or traumatic
  - Non- penetrating
  -
- Chronic:
  - Wound fails to heal in a reasonable amount of time
- Home work:
    - Avulsion, abrasion, crush injury

CLASSIFICATION OF WOUNDS:

- Clean
- Clean –contaminated
- Contaminated
- Infected or dirty

TYPE OF WOUND CLOSURE:

- Primary intention
- Delay primary intention
- Spontaneous or secondary intention
- Healing of partial-thickness wound

PRIMARY INTENTION

- Approximates the acutely disrupted tissue
- Applied to surgical wound or lacerations that closed with suture, staples, adhesion
- Heal by epithelialization
- Advantage:
  - rapid healing and return of function
  - Superior cosmetic result

DELAY PRIMARY INTENTION (TERTIARY)

- Approximation of the wound margins is delayed for several days after the wound occur
- Wound is initially manage as secondary intention after a matter (5 days) the wound edges approximated
- Used in traumatic wounds
- Advantage:
  - As in 1ry intention

SPONTANEOUS OR SECONDARY INTENTION

- When the wound edges are apart (full thickness tissue loss) or in highly contaminated wound
- Granulation tissue will form in the base of wound beside wound contraction

→to reduce wound area and allow epithelisation across the wound surface.

- Disadvantage:
  - poor functional and aesthetic result
  - Slower wound closure
  - Frequent dressing

HEALING OF PARTIAL-THICKNESS WOUND

- Loss of part of or all epidermis
- Healing through epithelialization

PHASES OF HEALING

- Inflammation [substrate]
  - Coagulation
- proliferative
  - Fibroplasia
  - Granulation
  - Contraction
  - epithelialization
- Remodeling [maturation]

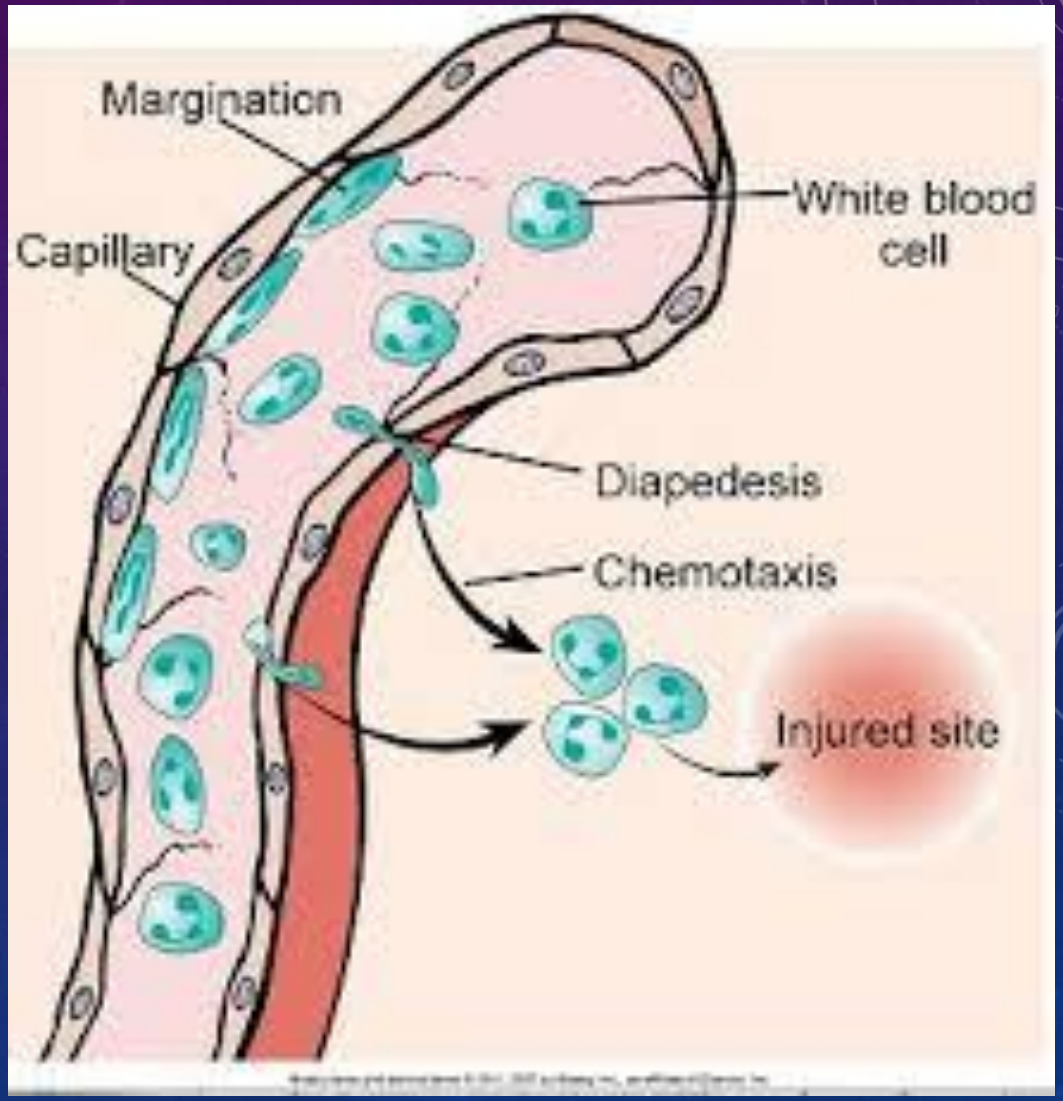
INFLAMMATORY PHASE

- hemostasis
  - At injury site, Lacerated vessels immediately constrict (5-10 min)
  - platelets aggregate and form hemostatic clot
  - The coagulation cascade initiated and the intrinsic and extrinsic coagulation pathways lead to activation of prothrombin → thrombin, which converts fibrinogen to fibrin (hemostatic and form scaffold that allows migration of infl. Cell and fibroblast)
  - Fibrin with its association glycoproteins vitronectin and fibronectin, forms the initial matrix for early wound healing (removal impedes wound healing)
  - Platelets degranulate releasing potent chemo-attractive for inflammatory cells (PDGF , TGF-β and chemokinase)
  - Release of bradykinin, serotonin, and histamine from tissue mast cells→ initiate the process of diapedesis and vasodilatation and vascular permeability (duration 72 hrs)

INFLAMMATORY PHASE

- The local endothelial cells break cell-cell contact and increase permeability and enhance Migration of leukocytes into the wound site.
- Within 24 h the wound predominated by polymorphonuclear leukocytes then within 48-72 h by monocytes (macrophages)
- Action:
  - Initial wound debridement :Remove necrotic debris , engulf foreign body, and attack infiltrating bacteria.
  - Macrophages will secrete growth factors that activate and attract local endothelial cells, fibroblasts and keratinocytes

- Cell migration:
  - Margination
  - adhesion
  - Diapedesis
  - Migration



Macrophage Activity	Activities During Wound Healing Mediators
Phagocytosis	Reactive oxygen species Nitric oxide
Débridement	Collagenase, elastase
Cell recruitment and activation	Growth factors: PDGF, TGF-, EGF, IGF Cytokines: TNF-, IL-1, IL-6 Fibronectin
Matrix synthesis	Growth factors: TGF-, EGF, PDGF Cytokines: TNF-, IL-1, IFN- Enzymes: arginase, collagenase Prostaglandins Nitric oxide
Angiogenesis	Growth factors: FGF, VEGF Cytokines: TNF- Nitric oxide

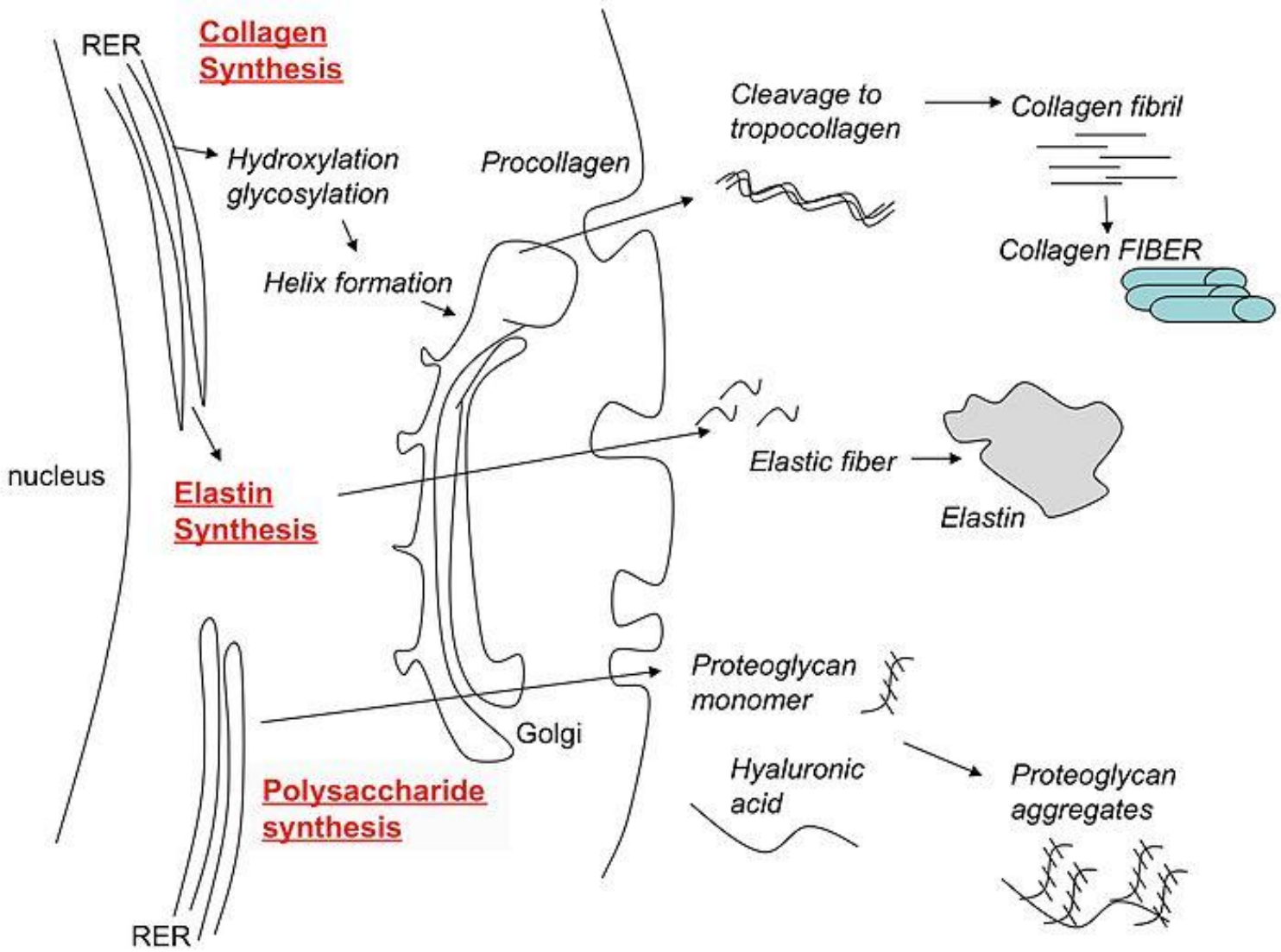
- Migration of PMN stops when wound contamination has been controlled
- Increase contamination stimulates PMN resulting to delayed wound healing and infection
- THE PMN is not crucial for normal healing , but macrophages is
- The initial response of the body to injury recognized by cardinal signs of inflammation:
  - Rubor (redness)
  - Colar (heat)
  - Tumor (swelling)
  - Dolar (pain)

PROLIFERATIVE PHASE

- Fibroplasia
  - Beginning at about 72 h after wounding
  - Fibroblast migrate into the wound and become the predominant cell in the wound by 3-5 day
  - Fibroblasts synthesized and secret extracellular matrix (ECM)
    - Collagen, fibronectin, elastin and proteoglycans.
  - The major fibrillar collagen composing the ECM in the skin and scar are collagen Type I and III (4:1)
  - Initially type III collagen deposit in relatively greater amount in the wound
  - The fibrous protein collagen is synthesized beside cross linking and deposition of collagen and other matrix protein. This will provide the healed wound with strength and integrity.

- Collagen is principal structural protein in the body.
- 19 different types of collagen are known
- The basic structural unit is right – handed triple helix
- Fibroblast synthesize and secrete collagens through complex intracellular and extracellular process
- Synthesis of collagen :
  - Started with production of amino acid chains in the cytoplasm of fibroblast
  - The α chains are unique in that each 3rd amino acid is glycine
  - Two amino acids, hydroxy-proline and hydroxy- lysine are found only in collagen , are required for hydroxylation
  - Procollagen formed and execreted from cell and cleaved to form tropocollagen
  - Crosslink of tropocollagen by lysyl oxidase to form fibrils then fibres.

Synthesis and Assembly of CT components



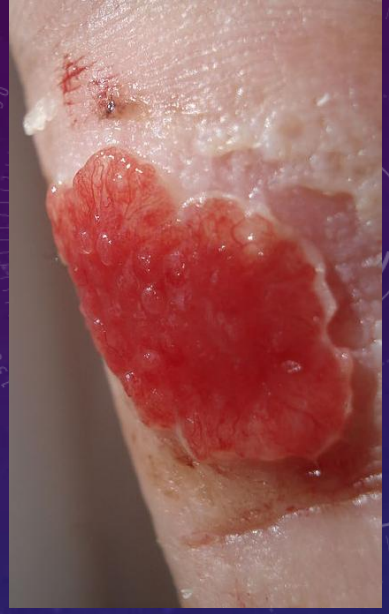
EPITHELIALIZATION

- It restores the barrier between the wound and external environment
- Mobilization :
  - Loss of contact inhibition of the epithelial cells, basal cells at wound edge and from remaining skin appendages flatten and break contact (integrins) with neighboring cells and dermis
- Migration
  - Cells move across wound until meeting cells from other sides, then contact inhibition reestabilished
- Mitosis
  - As cells at edges migrating , basal cells from wound edges proliferate to support cell numbers needed to bridge wound
- Differentiation
  - Reestablishment of epithelial layers after migration ceases

CONTRACTION

- Defined as the centripetal movement of wound edges to facilitate closure of wound defect
- The size of the wound becomes gradually smaller by mechanism of circumferential contraction of collagen
- Myofibroblast:
  - specialized fibroblast with contractile cytoplasmic microfilaments and distinct cellular adhesion structure.
  - Appear day 3 , are maximal at day 10-21
  - Distributed throughout granulating wound and contract entire wound bed
  - Whereby myofibroblast shorten the wound, followed by collagen deposition and cross linking to maintain the contraction

GRANULATION



- **Granulation tissue** is new connective tissue and tiny blood vessels that form on the surfaces of a wound during the healing process
- Granulation tissue consists of new blood vessels, fibroblasts, inflammatory cells, endothelial cells, myofibroblasts, and the components of a new, provisional extracellular matrix (ECM)
- begins to appear in the wound already during the inflammatory phase, two to five days post wounding, and continues growing until the wound bed is covered

REMODELING [MATURATION]

- It is a dynamic process in terms of cellular composition and the organization of matrix molecules.
- During 2-3wk the increased density of inflammatory cells and angiogenesis begins to resolve by apoptosis .
- The equilibrium between collagen synthesis and degradation (by collagenase) is gradually restored beside more organized and cross-linked collagen fibrils
- This phase may last from many months to 2 yr, increase the strength of wound up to 70% of normal.

GROWTH FACTORS IN WOUND HEALING

- They are polypeptides that function to regulate the wound healing response

GROWTH FACTORS IN WOUND HEALING

Table 8-2 Growth Factors Participating in Wound Healing

Growth Factor	Wound Cell Origin	Cellular and Biological Effects
Platelet-derived growth factor (PDGF)	Platelets, macrophages, monocytes, smooth muscle cells, endothelial cells	Chemotaxis: fibroblasts, smooth muscle, monocytes, neutrophils
		Mitogenesis: fibroblasts, smooth muscle cells
		Stimulation of angiogenesis
		Stimulation of collagen synthesis
Fibroblast growth factor (FGF)	Fibroblasts, endothelial cells, smooth muscle cells, chondrocytes	Stimulation of angiogenesis (by stimulation of endothelial cell proliferation and migration)
		Mitogenesis: mesoderm and neuroectoderm
		Stimulates fibroblasts, keratinocytes, chondrocytes, myoblasts

Keratinocyte growth factor (KGF)	Keratinocytes, fibroblasts	Significant homology with FGF; stimulates keratinocytes
Epidermal growth factor (EGF)	Platelets, macrophages, monocytes (also identified in salivary glands, duodenal glands, kidney, and lacrimal glands)	Stimulates proliferation and migration of all epithelial cell types
Transforming growth factor- B (TGF- B)	Keratinocytes, platelets, macrophages	Homology with EGF; binds to EGF receptor
		Mitogenic and chemotactic for epidermal and endothelial cells
Transforming growth factor- alpha (TGF- alpha) (3 isoforms: 1’ 2’ 3)	Platelets, T lymphocytes, macrophages, monocytes, neutrophils	Stimulates angiogenesis TGF- 1 stimulates wound matrix production (fibronectin, collagen glycosaminoglycans); regulation of inflammation
		TGF- 3 inhibits scar

Table 8-2 Growth Factors Participating in Wound Healing

Insulin-like growth factors (IGF-1, IGF-2)	Platelets (IGF-1 in high concentrations in liver; IGF-2 in high concentrations in fetal growth)	Likely the effector of growth hormone action
		Promotes protein/extracellular matrix synthesis
		Increase membrane glucose transport
Vascular endothelial growth factor (VEGF)	Macrophages, fibroblasts, keratinocytes	Similar to PDGF
		Mitogen for endothelial cells (not fibroblasts)
		Stimulates angiogenesis
Granulocyte-macrophage colony-stimulating factor (GM-CSF)	Macrophage/monocytes, endothelial cells, fibroblasts	Stimulates macrophage differentiation/proliferation

FACTORS AFFECT WOUND HEALLING

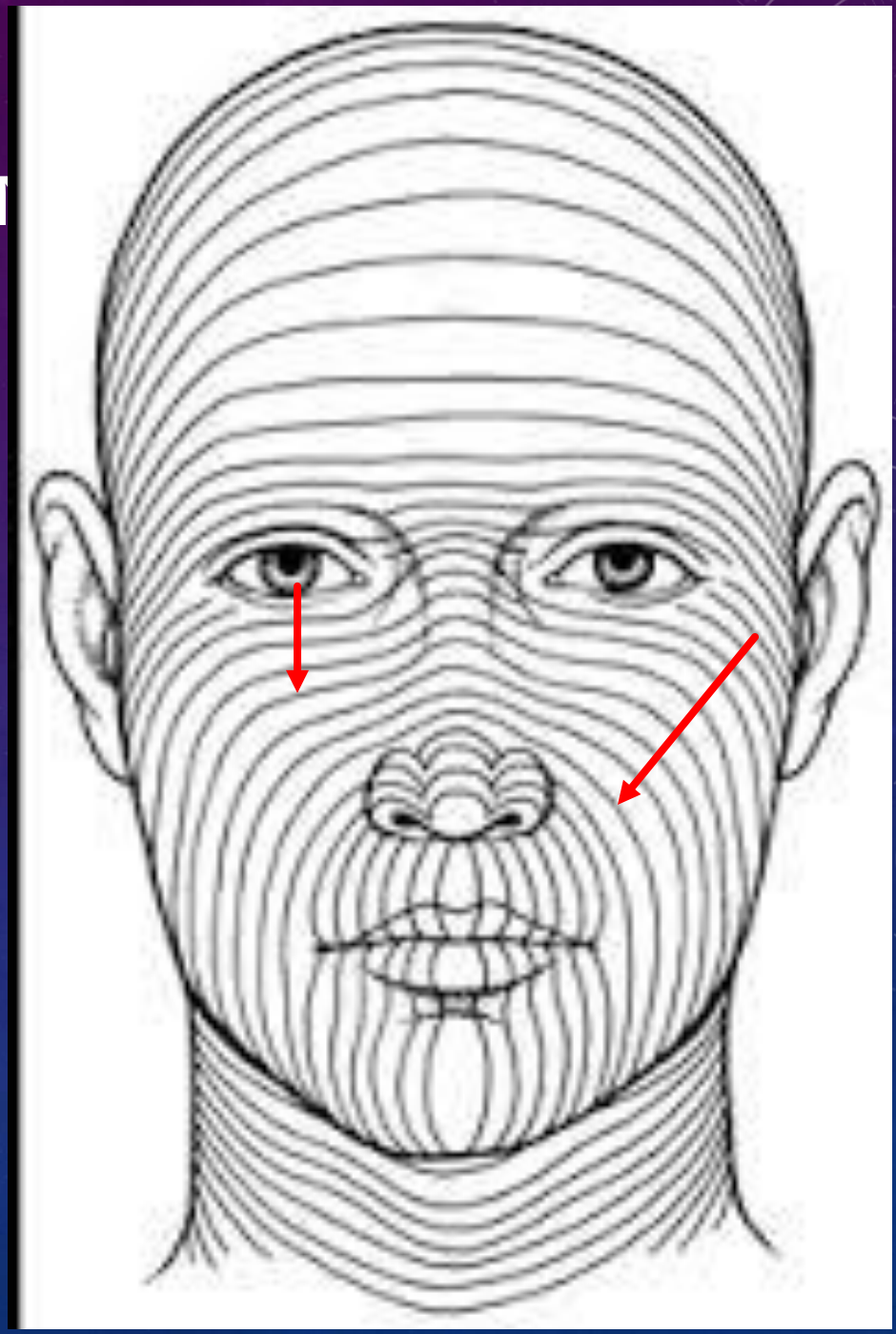
- Local factors
  - Hypoxia and ischemia
    - Lead to impair collagen synthesis
    - Prevent fibroblast migration
    - Increase susceptibility to the wound infection
  - Infection
    - Delay wound healing
    - Increase tissue destruction
  - Presence of foreign body and necrotic tissue
    - Prolonging the inflammatory phase
    - Predispose
  - Irradiation
  - Venous insufficiency

- Systemic factors
  - Malnutition
    - Vit C deficiency
    - Vit A
    - Protein
  - Co morbidity
    - DM
    - Renal and liver disease
  - Steroid and immunosuppression
  - Smoking

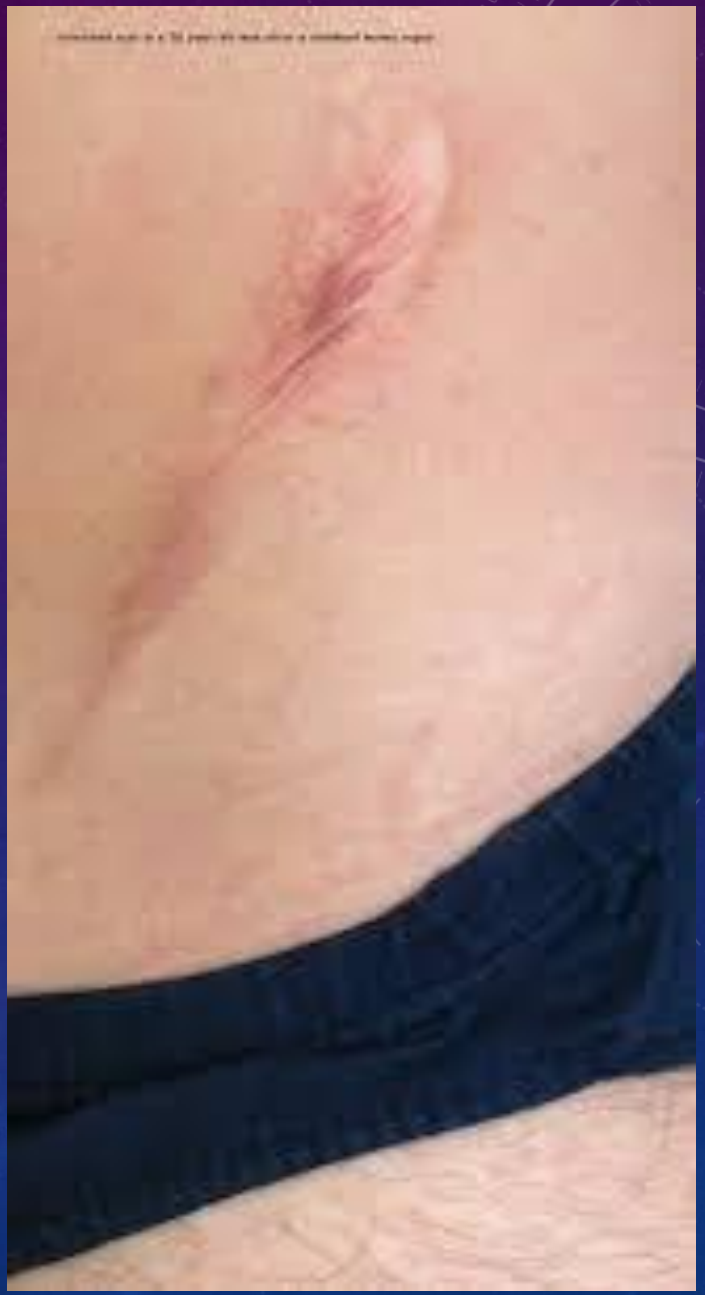
SCARS

- many of which can be avoided or prevented by correct incision planning and adequate wound management. Some types, however, cannot be prevented and are unpredictable in their occurrence
- The appearance of some scars can be improved by surgical or other means, but scars can never be removed totally
- **Adverse scar**
  - Wrong direction
  - Stretched scar
  - Contracted scar
  - Pigment alteration
  - Hypertrophic scars and keloid scars
  - Contour deformity
  - Tattooing
  - Stitch marks

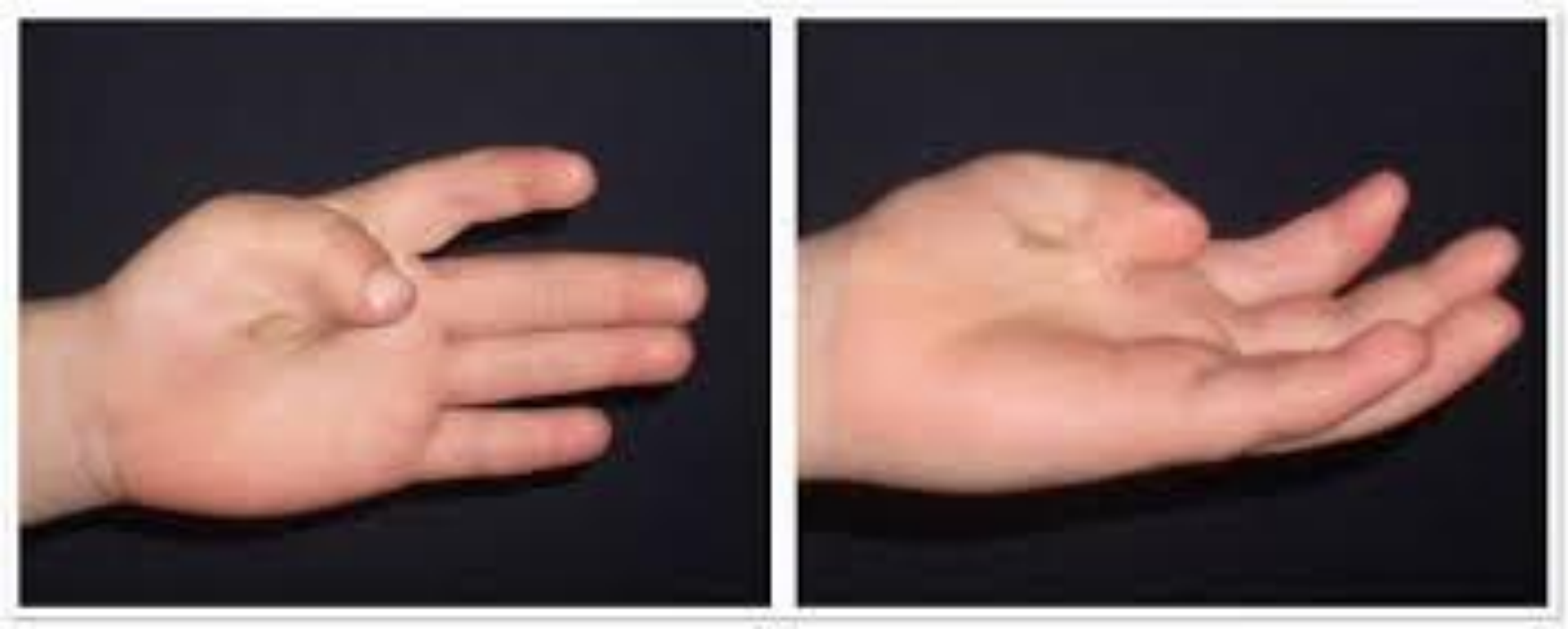
WRONG DIRECTIOI



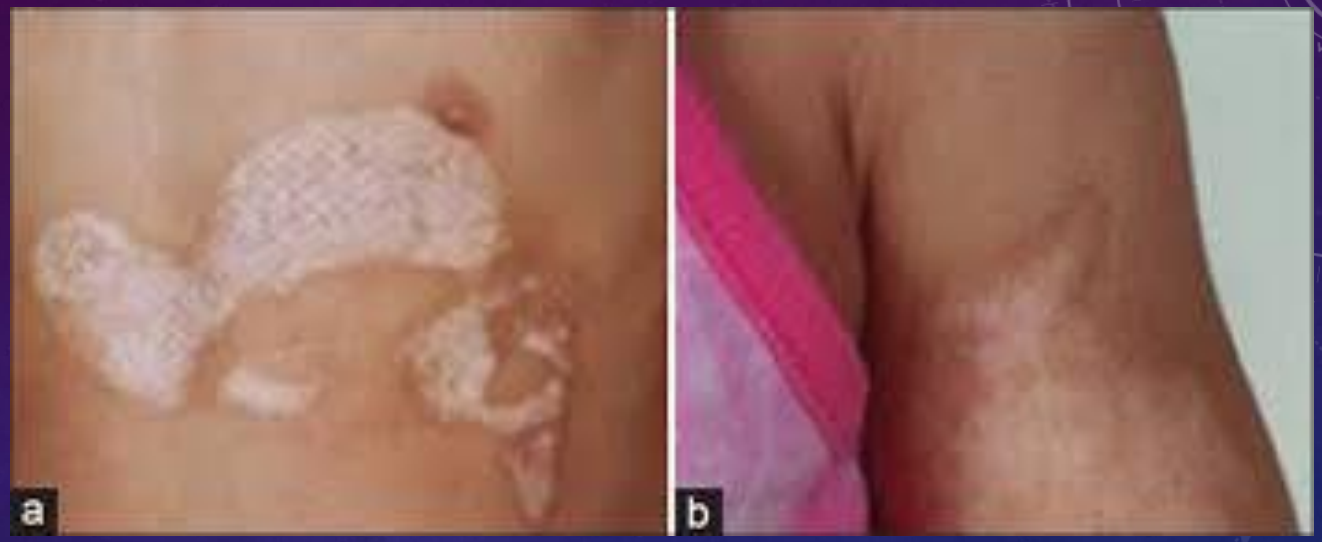
STRETCHED SCAR



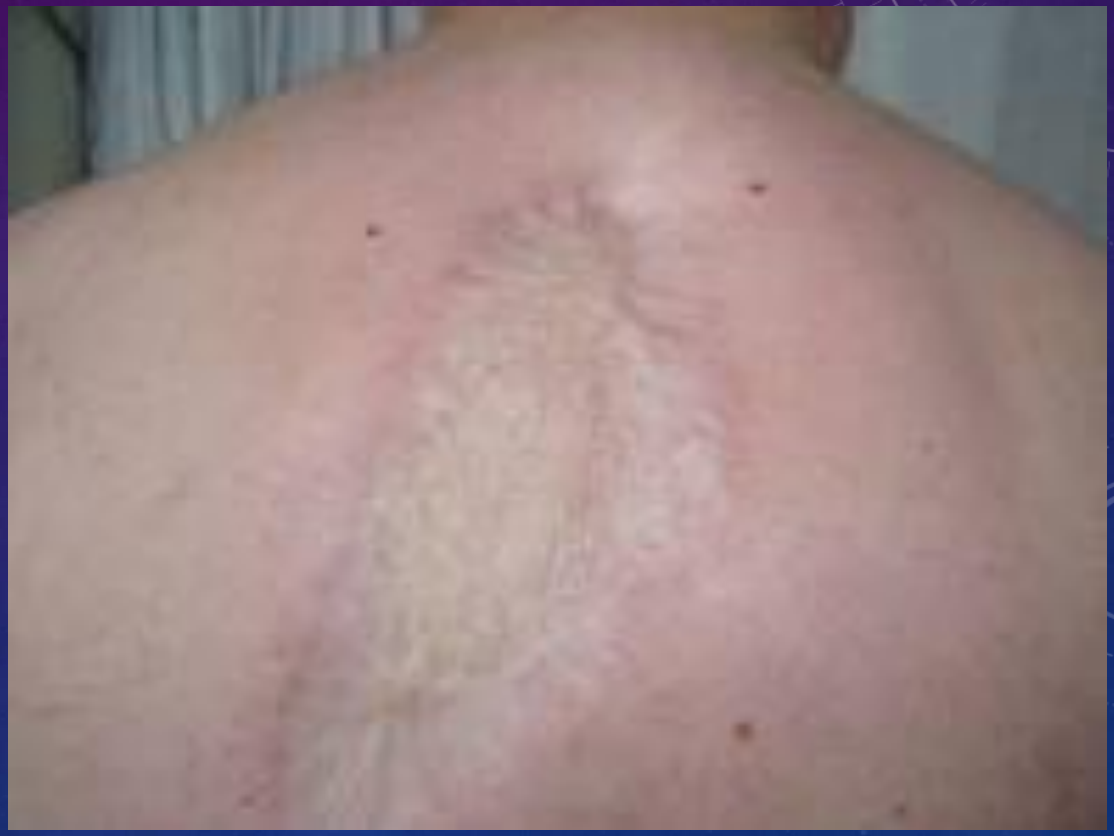
CONTRACTED SCAR



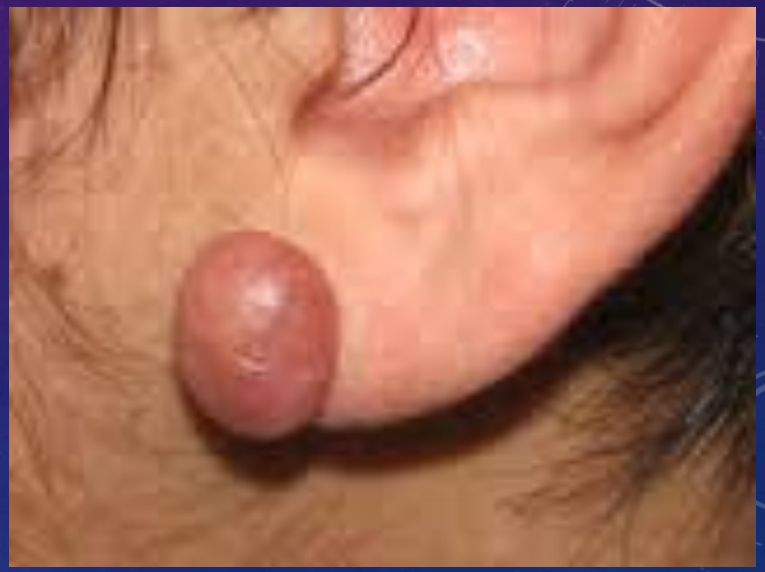
PIGMENT ALTERATION



CONTOUR DEFORMITY



HYPERTROPHIC SCARS AND KELOID SCARS



HYPERTROPHIC SCARS AND KELOID SCARS

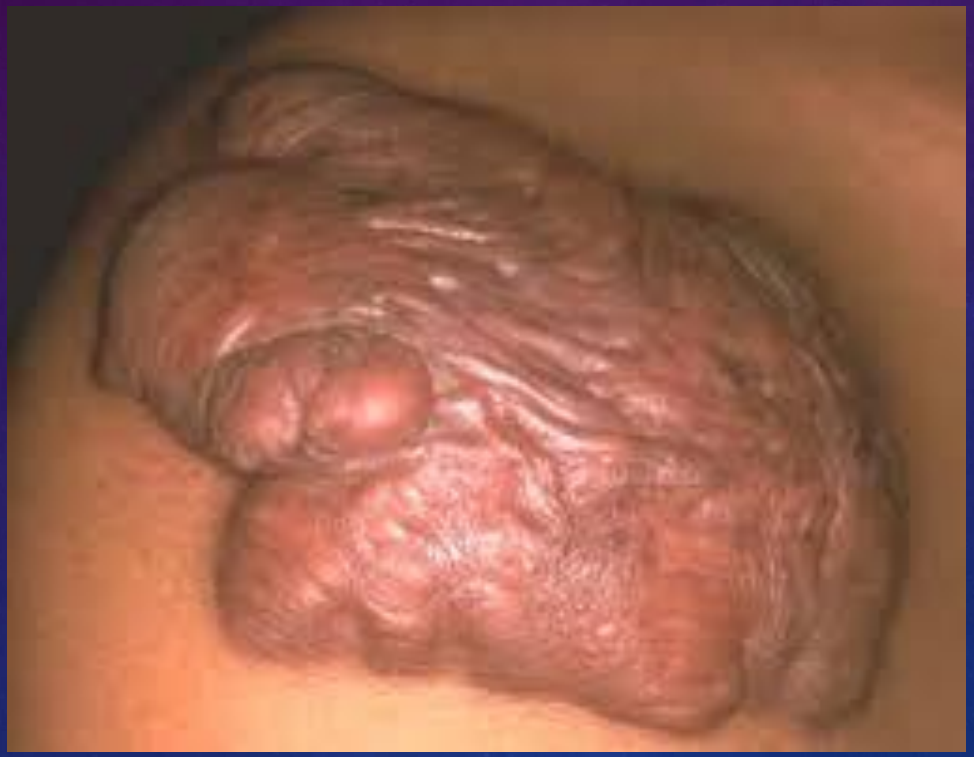
Features	*Hypertrophic scar*	*Keloid scar*
Genetic	Not familial	May be familial
Race	Not race related	Black > white
Sex	Female = male	Female > male
Age	Children	10–30 years
Borders	Remains within wound	Outgrows wound area
Natural history	Subsides with time	Rarely subsides
Site	Flexor surfaces	Sternum, shoulder, face
Aetiology	Related to tension	Unknown

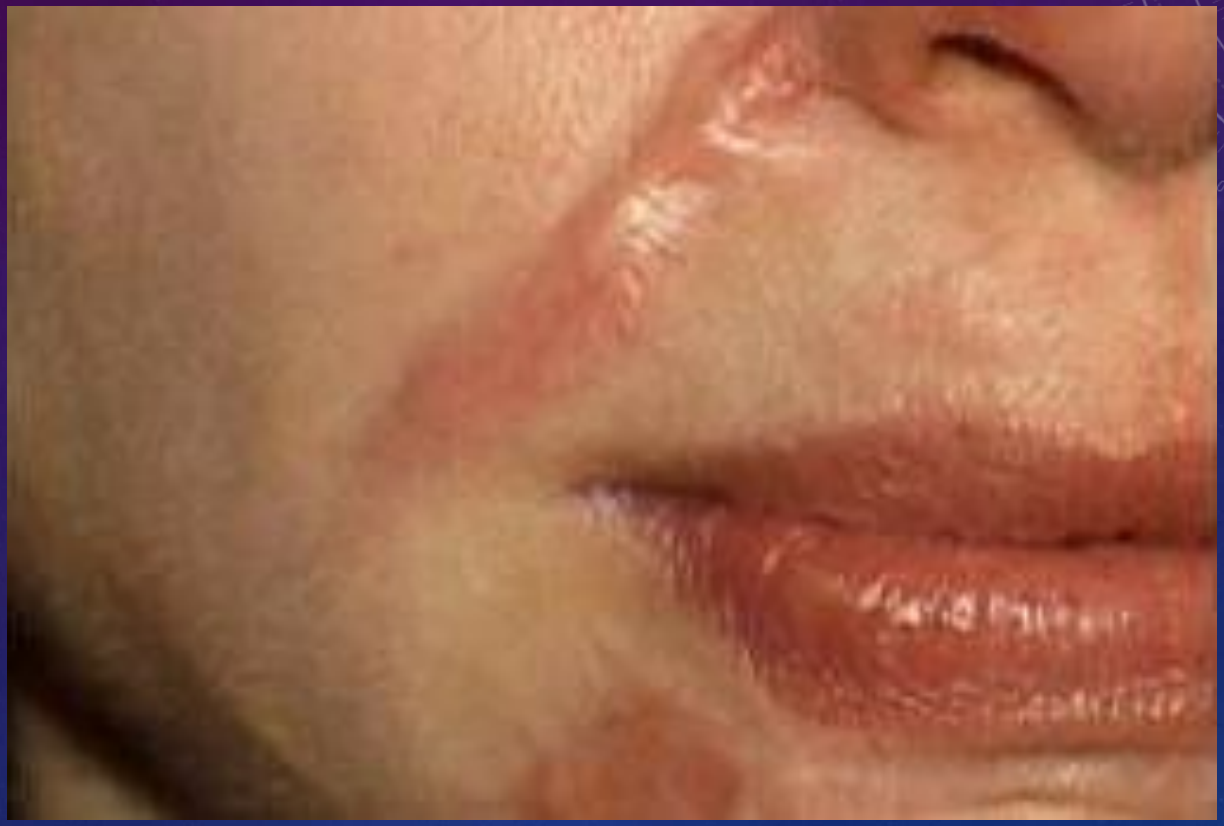
HYPERTROPHIC SCARS AND KELOID SCARS

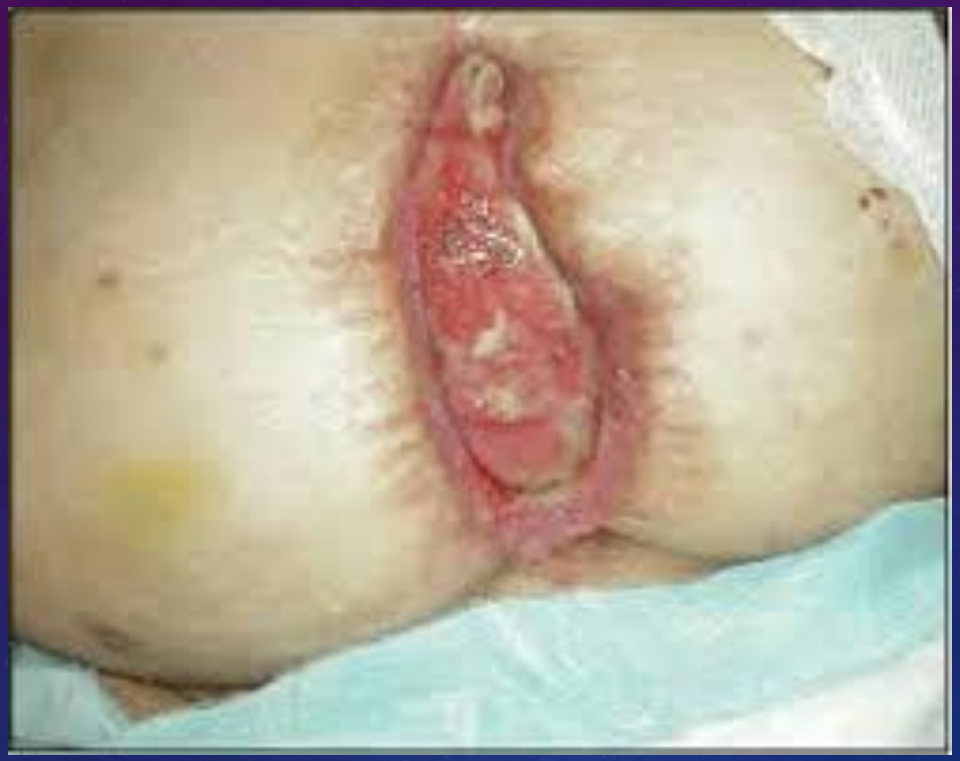
Hypertrophic Scars	Keloids
Develop soon after surgery	May develop months after the trauma
Usually improve with time	Rarely improve with time
Remain within the confines of the wound	Spread outside the boundaries of the initial lesion
Occur when scar cross joints or skin creases at a right angle	Occur predominantly on the ear lobe, shoulders, sternal notch, rarely across joints
Improve with appropriate surgery	Are often worsened by surgery
Frequent incidence	Rare incidence
Have no association with skin color	Associated with dark skin color

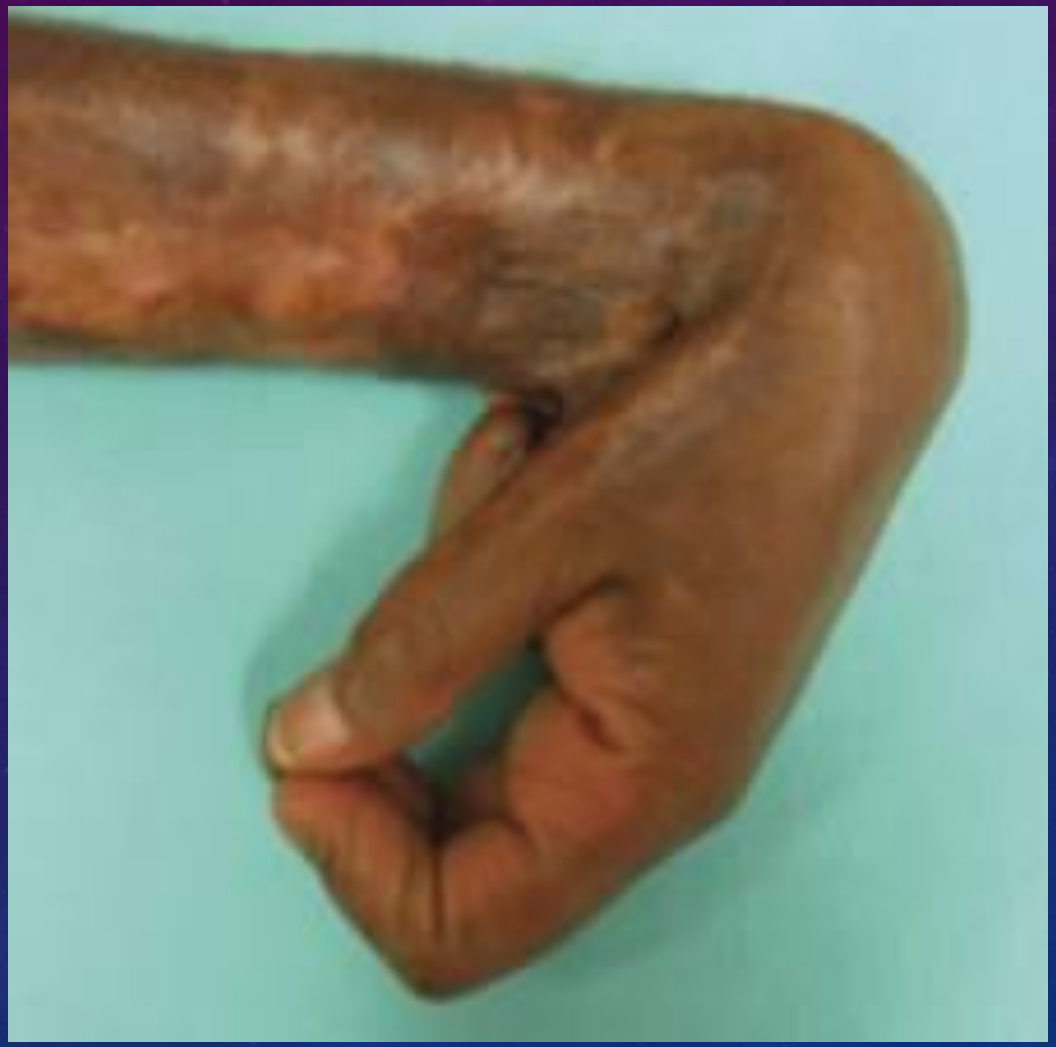
WOUND ASSESSMENT

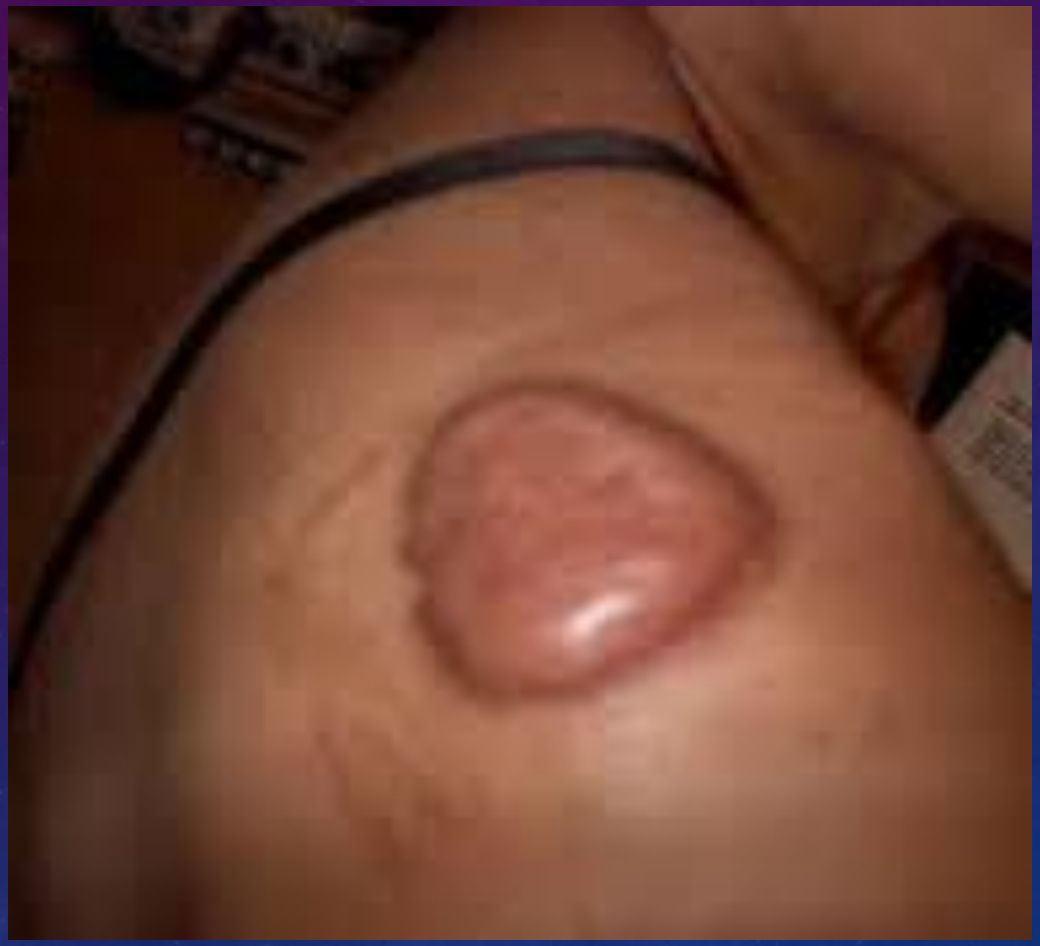
- History:
- Examination
- Wound evaluation:
  - Location
  - Size: length,width, depth, and area
  - Extent of the defect: skin , subcutaneous, muscle, tendon, bone, nerve
  - Condition of surrounding tissue and wound margins
    - Color, pigmentation, induration ,edema
  - Condition of wound bed
    - Order, necrosis, granulation tissue, exudate , eschar.

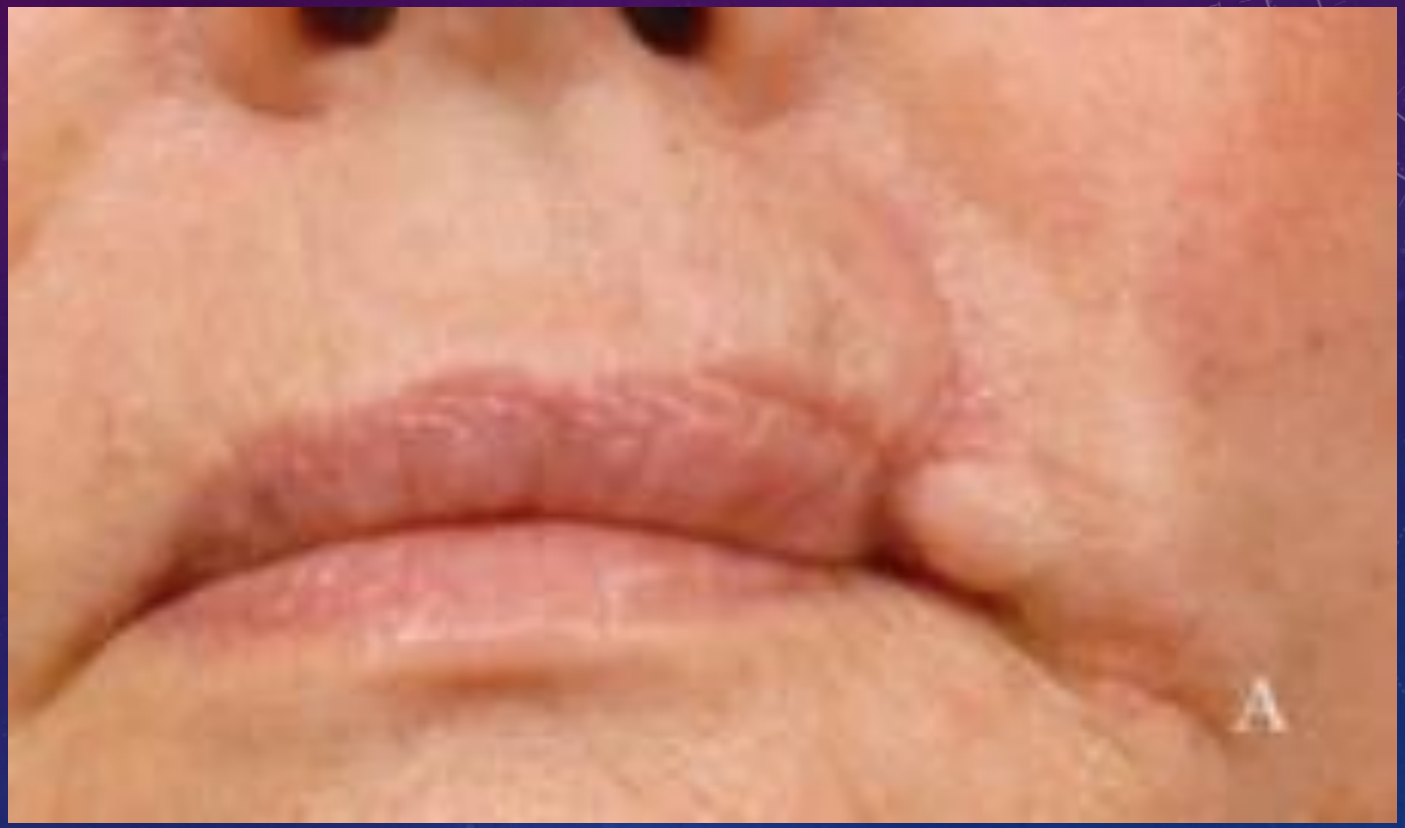








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